L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:310872 CAPLUS Full-text
DN 140:321159
TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive agents
IN Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan; Berstein, David L.
PA USA
SO U.S. Pat. Appl. Publ., 55 pp., Cont.-in-part of U.S. Pat. Appl. 2003 220,297.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004073024	A1	20040415	US 2003-635054	20030806
	US 2003220297	A1	20031127	US 2003-357152	20030203
	US 2005032825	A1	20050210	US 2004-862149	20040604
PRAI	US 2002-353252P	P	20020201		
	US 2002-426928P	P	20021115		
	US 2002-428383P	P	20021122		
	US 2002-433930P	P	20021217		
	US 2003-357152	A2	20030203		
	US 2003-635054	A2	20030806		

OS MARPAT 140:321159
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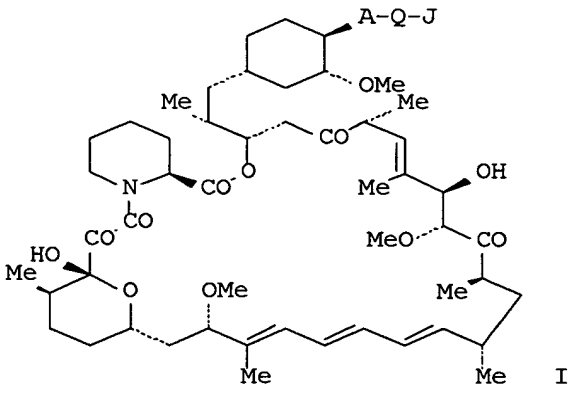


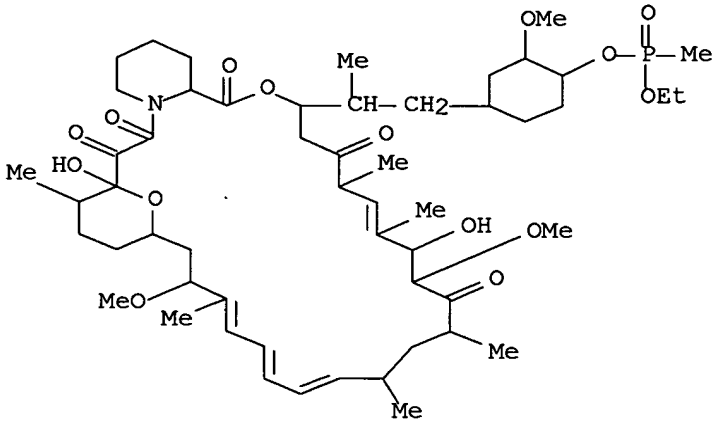
I

AB Rapamycin derivs. containing a phosphorus moiety, such as I [A = O, S, NR2; Q = bond, aliphatic, heteroaliph., aryl, or heteroaryl moiety; J = P(O)(R5)2, P(O)(R5)(OR5). P(O)(R5)(NR2R5), P(O)(NR2R5)2, P(O)(OR5)(NR2R5); R2, R5 = H, aliphatic, heteroaliph., heteroaryl, etc.], were prepared for therapeutic use as immunosuppressive agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-Q-J = OP(O)(OEt)(Me)] was prepared by

reacting rapamycin with Et methylphosphonochloridate using 3,5-lutidine in CH2Cl2 under a nitrogen atmospheric Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IT **572924-46-0P 572924-47-1P 572924-48-2P**
572924-49-3P 572924-50-6P 572924-51-7P
572924-52-8P 572924-53-9P 572924-54-0P
572924-55-1P 572924-56-2P 572924-57-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive agents)

RN 572924-46-0 CAPLUS
CN Rapamycin, 42-(ethyl methylphosphonate) (9CI) (CA INDEX NAME)



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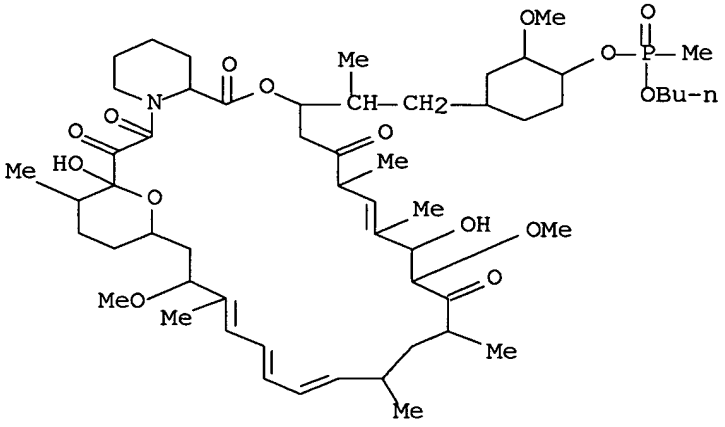

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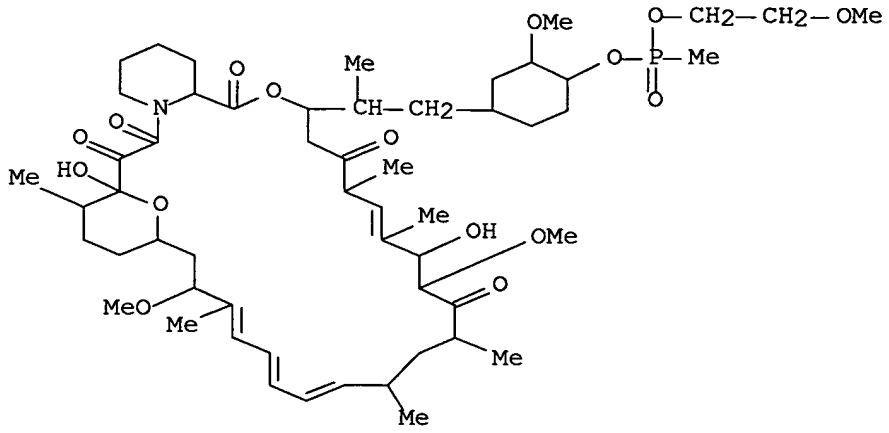

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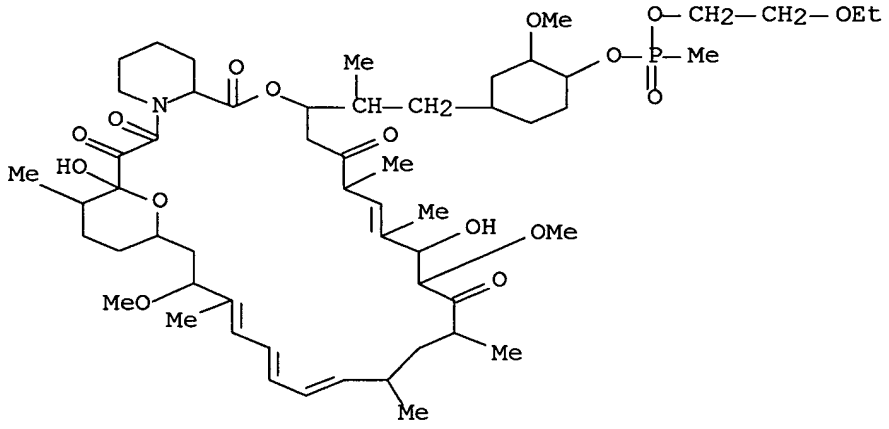

RN 572924-50-6 CAPLUS
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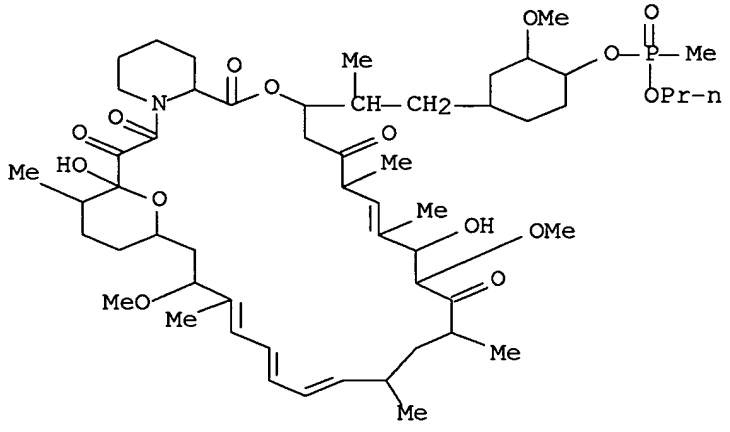

RN 572924-51-7 CAPLUS
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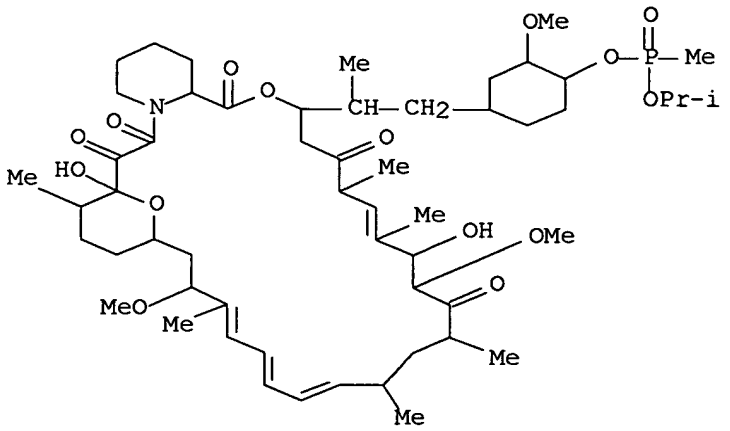
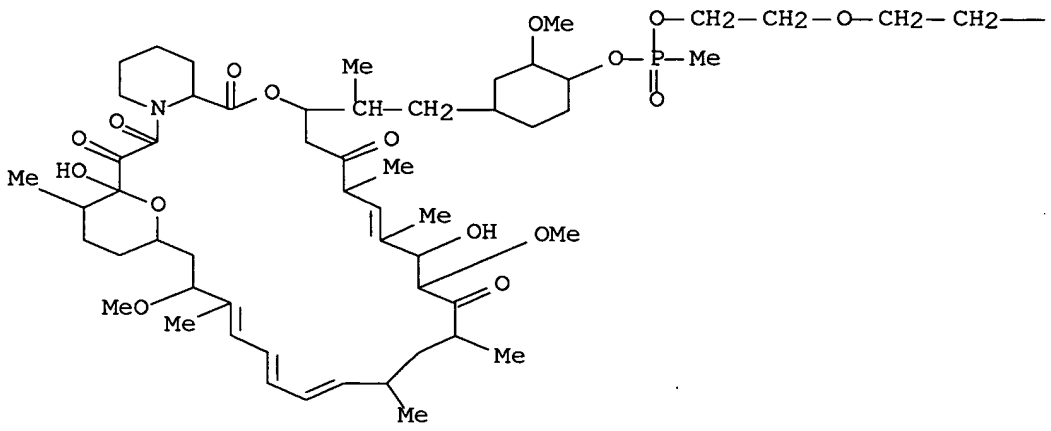


RN 572924-52-8 CAPLUS
CN Rapamycin, 42-[2-(2-hydroxyethoxy)ethyl methylphosphonate] (9CI) (CA INDEX NAME)

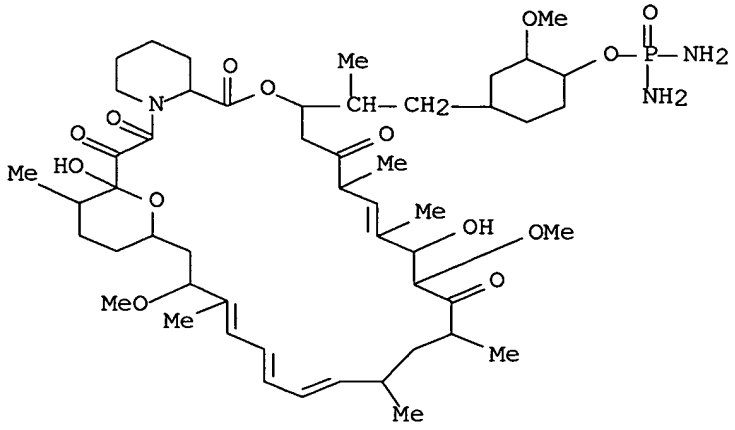
PAGE 1-A



PAGE 1-B

—OH

RN 572924-53-9 CAPLUS
CN Rapamycin, 42-phosphorodiamidate (9CI) (CA INDEX NAME)



RN 572924-54-0 CAPLUS
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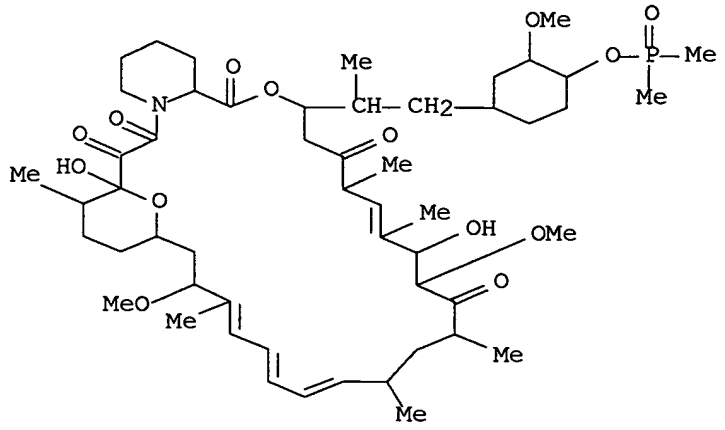

RN 572924-55-1 CAPLUS
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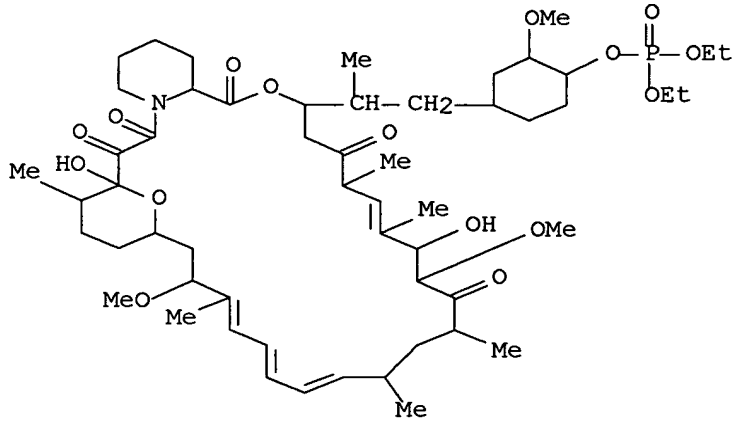

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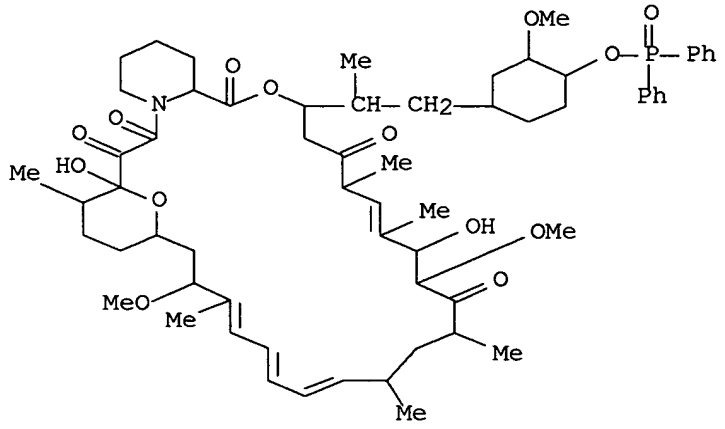

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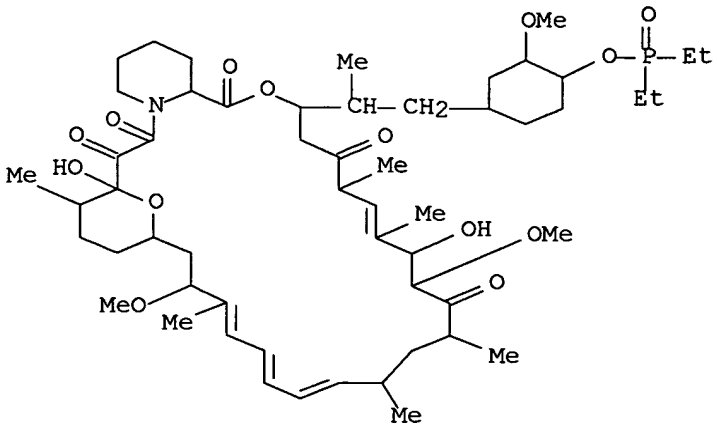
CN Rapamycin, 42-(diethyl phosphinate) (9CI) (CA INDEX NAME)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CH—CH2
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L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:610416 CAPLUS Full-text
DN 139:149459
TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive agents
IN Berstein, David L.; Metcalf, Chester A., III; Rozamus, Leonard W.; Wang, Yihan
PA Ariad Gene Therapeutics, Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003064383	A2	20030807	WO 2003-US3030	20030203
	WO 2003064383	A3	20040122		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1478648	A2	20041124	EP 2003-735110	20030203
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PRAI	US 2002-353252P	P	20020201		
	US 2002-426928P	P	20021115		
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OS MARPAT 139:149459
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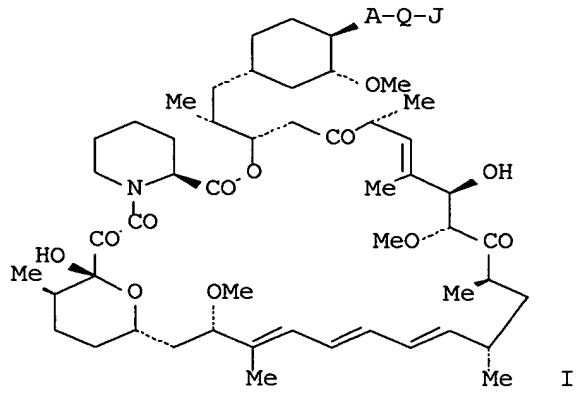


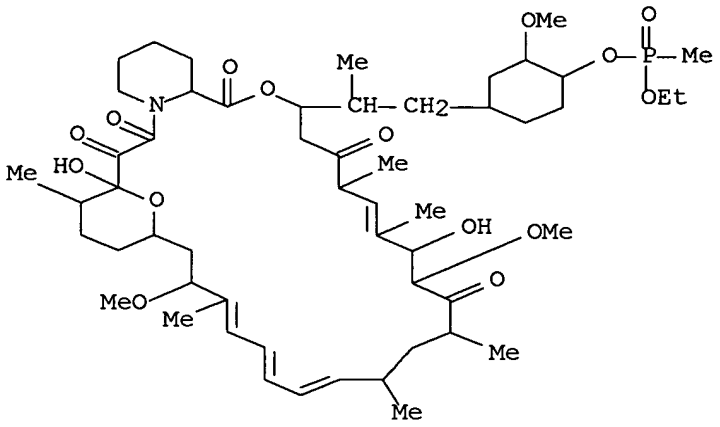
I

AB Rapamycin derivs. containing a phosphorus moiety, such as I [A = O, S, NR2; Q = bond, aliphatic, heteroaliph., aryl, or heteroaryl moiety; J = P(O)(R5)2, P(O)(R5)(OR5). P(O)(R5)(NR2R5), P(O)(NR2R5)2, P(O)(OR5)(NR2R5); R2, R5 = H, aliphatic, heteroaliph., heteroaryl,

etc.], were prepared for therapeutic use as immunosuppressive agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-Q-J = OP(O)(OEt)(Me)] was prepared by reacting rapamycin with Et methylphosphonochloridate using 3,5-lutidine in CH2Cl2 under a nitrogen atmospheric Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IT **572924-46-0P 572924-47-1P 572924-48-2P**
572924-49-3P 572924-50-6P 572924-51-7P
572924-52-8P 572924-53-9P 572924-54-0P
572924-55-1P 572924-56-2P 572924-57-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive agents)

RN 572924-46-0 CAPLUS
CN Rapamycin, 42-(ethyl methylphosphonate) (9CI) (CA INDEX NAME)



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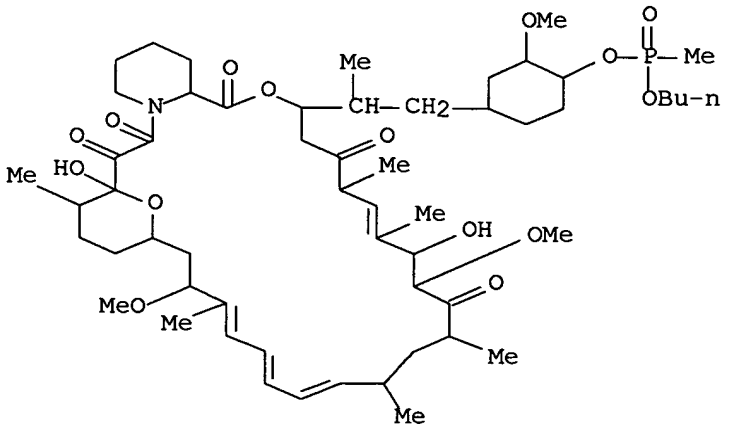

RN 572924-48-2 CAPLUS
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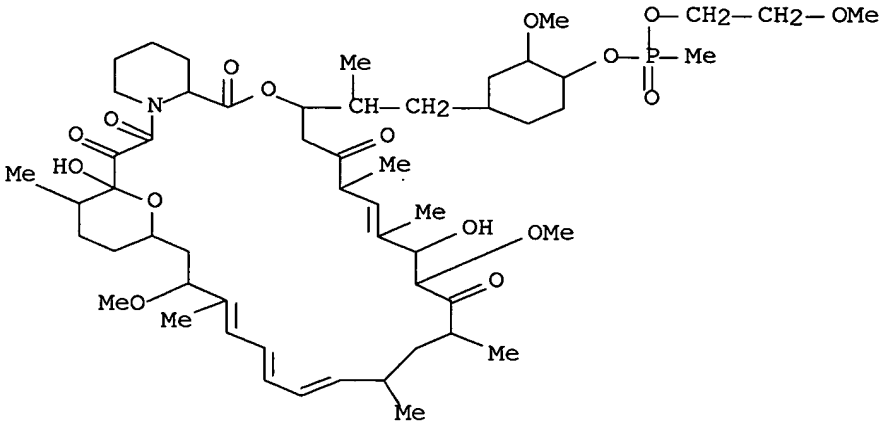

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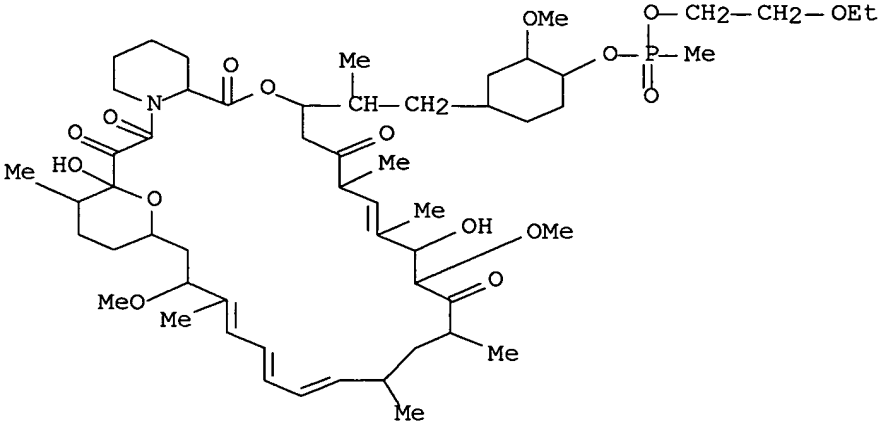

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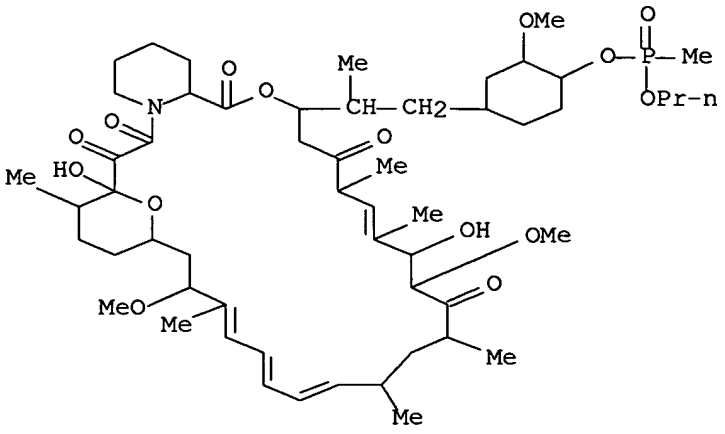

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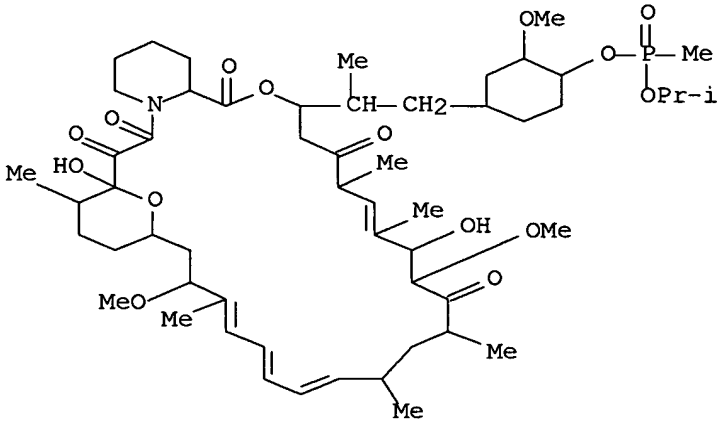
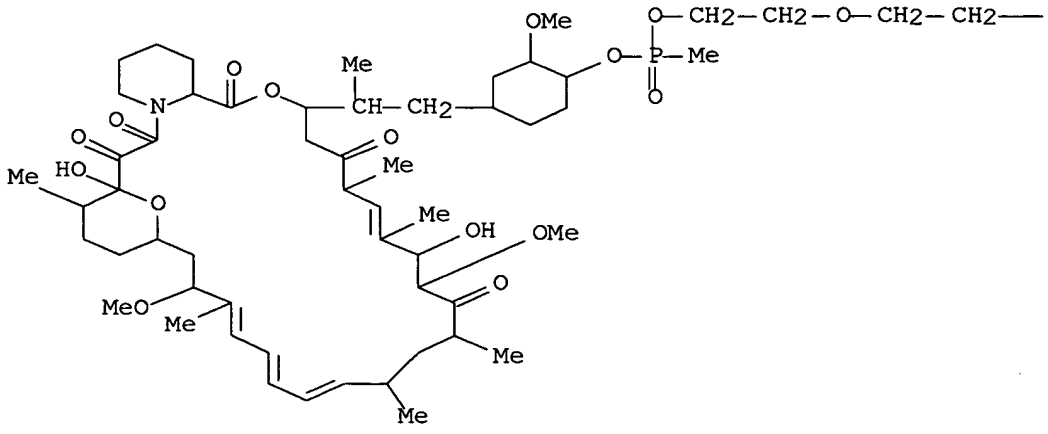


RN 572924-52-8 CAPLUS
CN Rapamycin, 42-[2-(2-hydroxyethoxy)ethyl methylphosphonate] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

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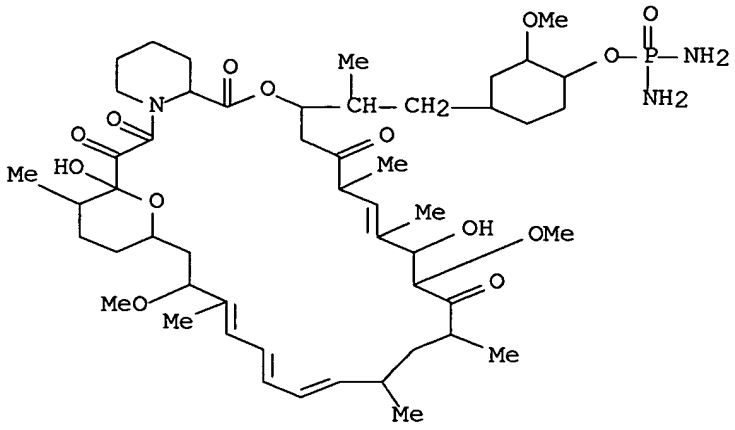
RN 572924-53-9 CAPLUS
CN Rapamycin, 42-phosphorodiamidate (9CI) (CA INDEX NAME)



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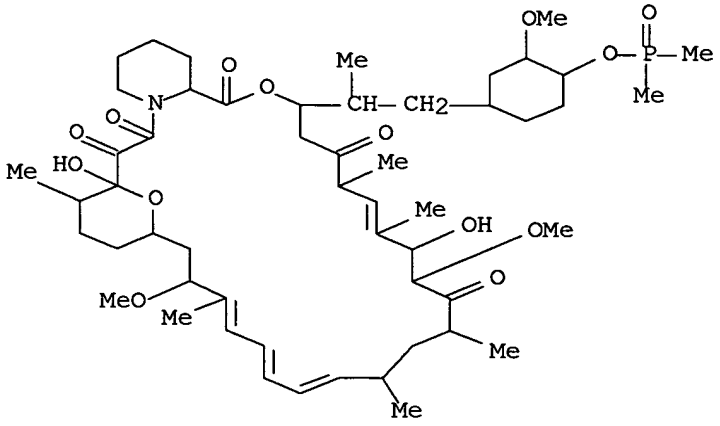

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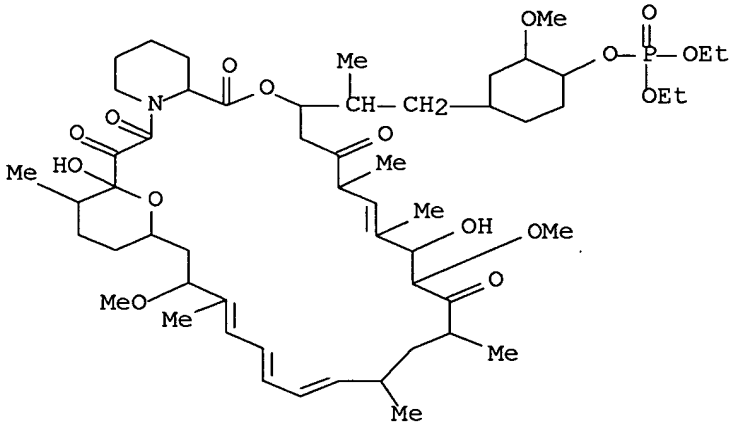

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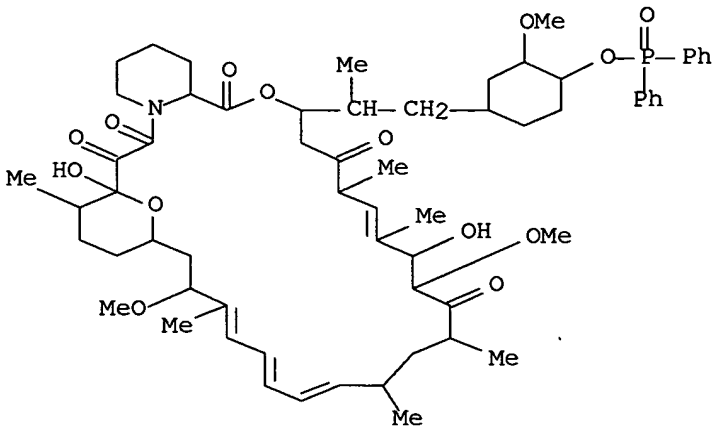

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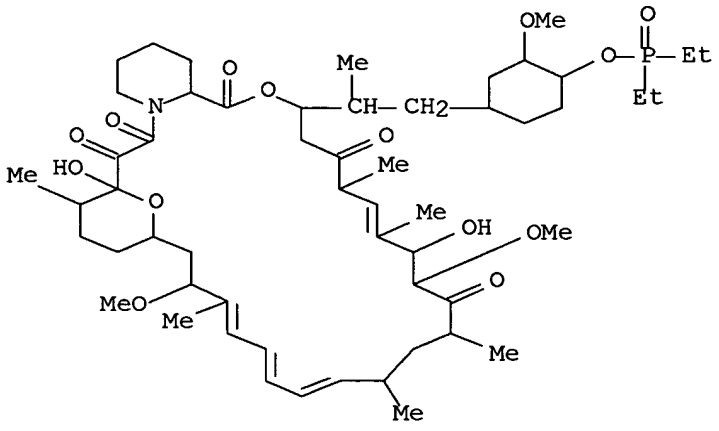
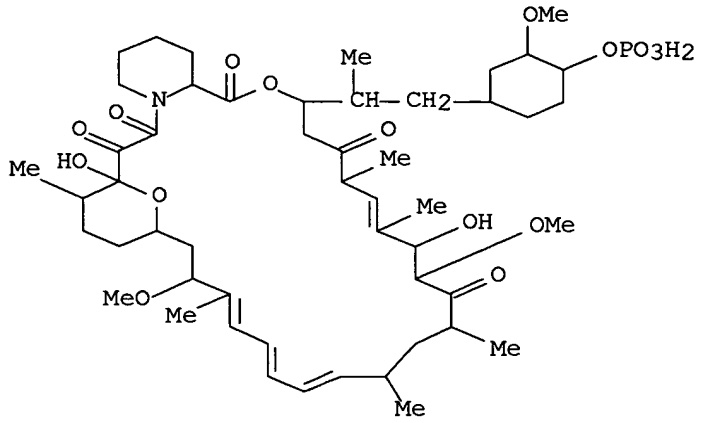


L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:681128 CAPLUS Full-text
DN 128:1765
TI Microbial conversion of rapamycin
AU Kuhnt, Michaela; Bitsch, Francis; Ponelle, Monique; Fehr, Theo; Sanglier, Jean-Jacques
CS Preclinical Research, Novartis Pharma Ltd., Basel, CH4002, Switz.
SO Enzyme and Microbial Technology (1997), 21(6), 405-412
CODEN: EMTED2; ISSN: 0141-0229
PB Elsevier
DT Journal
LA English
AB In order to obtain derivs. of rapamycin, a total of 28 bacterial and 72 fungal strains were screened for their ability to transform rapamycin. In the course of this screening, the already known derivs. 39-O-demethylrapamycin, 27-O-demethylrapamycin, 16-O-demethylrapamycin, and the 40-O-phosphoric ester of rapamycin were detected and isolated out of fermns. with Streptomyces rimosus ATCC 28893 or Thamnidium elegans ATCC 8997. Biotransformation of rapamycin using Syncephalastrum racemosus ATCC 1332B, Gliocladium deliquescens ATCC 10097, or Bacillus subtilis ATCC 55060 yielded the conversion products 24-hydroxyrapamycin, secorapamycins A, B, and C, and 16-O-demethylsecorapamycin B. None of these derivs. exhibited a stronger immunosuppressive effect than the parent compound; however, in the case of 24-hydroxyrapamycin and 40-O-phosphoric ester of rapamycin, a FKBP-binding affinity comparable to rapamycin was observed
IT **143715-59-7P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)(microbial conversion of rapamycin)
RN 143715-59-7 CAPLUS
CN Rapamycin, 42-phosphate (9CI) (CA INDEX NAME)

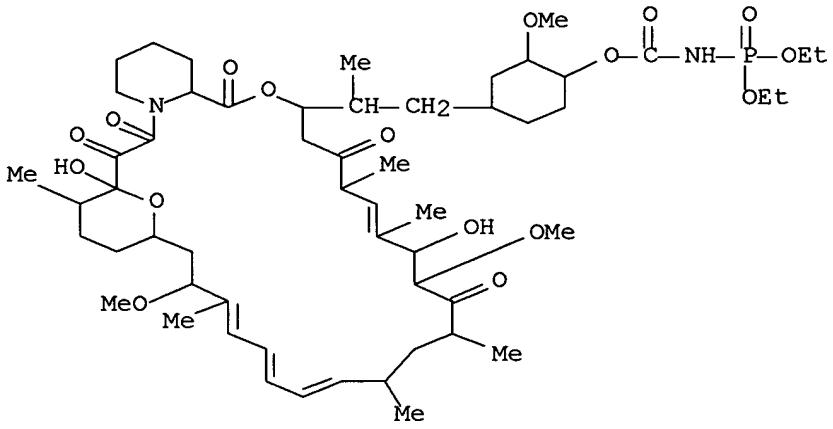


RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:605544 CAPLUS Full-text
DN 123:9263
TI Phosphorylcarbamates of rapamycin and their oxime derivatives
IN Skotnicki, Jerauld S.; Smith, Andri L.
PA American Home Products Corporation, USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5391730	A	19950221	US 1993-134428	19931008
	US 5455249	A	19951003	US 1994-327335	19941021
PRAI	US 1993-134428	A3	19931008		

OS MARPAT 123:9263
AB 31,42-Diesters and 42-monoesters of rapamycin with phosphinyl isocyanates and their 27-oximes were prepared Thus, rapamycin was treated with 1 equivalent of (EtO)2PNCO to give 36% of the 42-(diethoxyphosphoryl)carbamate which had an IC50 for inhibition of lymphocyte proliferation of 10.0 nM.
IT **163714-67-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP(Preparation); USES (Uses)(phosphorylcarbamates of rapamycin and their oxime derivs. as immunosuppressants)
RN 163714-67-8 CAPLUS
CN Rapamycin, 42-[(diethoxyphosphinyl)carbamate] (9CI) (CA INDEX NAME)

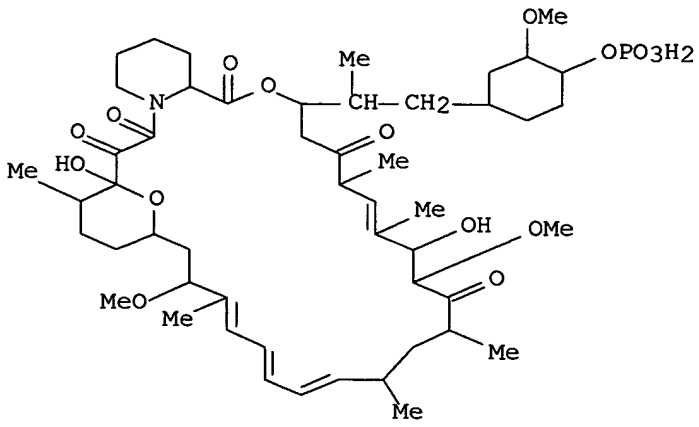


L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:146230 CAPLUS Full-text
DN 118:146230
TI Process for biophosphorylating organic compounds
IN Chen, Shieh Shung Tom; Petuch, Brian R.; Hsu, Annjia T.; Arison, Byron H.; Dumont, Francis; White, Raymond F.; Mathre, David J.; Wu, Jane T.; So, Lydia T.; Reamer, Robert A.
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9206992	A2	19920430	WO 1991-US6816	19910919
	WO 9206992	A3	19920625		
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5198421	A	19930330	US 1991-691606	19910426
	CA 2093429	AA	19920410	CA 1991-2093429	19910919
	EP 552309	A1	19930728	EP 1992-901105	19910919
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06502536	T2	19940324	JP 1992-501234	19910919
PRAI	US 1990-594214	A2	19901009		
	US 1990-594500	A	19901009		
	US 1990-595894	A	19901011		
	US 1991-691606	A	19910426		
	US 1991-691607	A	19910426		
	US 1991-701387	A	19910516		
	US 1991-735963	A	19910725		
	WO 1991-US6816	W	19910919		

AB Phosphorylated organic compds. are prepared by incubating the hydroxyl-containing organic compds. such as FK506-type macrolides with Rhizopus oryzae, or echinocandins with R. arrhizus. By this process inflammation inhibitors, HIV protease inhibitors, and compds. with immunoregulatory activity can be prepared C-32 phosphorylated FK-506 was prepared from FK-506 with R. oryzae and tested for its ability to inhibit T cell proliferation. The organic synthesis of various bioactive compds., their biophosphorylation and testing for biol. activity, and formulation are described.

IT **143715-59-7P**
RL: PREP (Preparation)
(preparation of, by biophosphorylation with Rhizopus oryzae)
RN 143715-59-7 CAPLUS
CN Rapamycin, 42-phosphate (9CI) (CA INDEX NAME)


OMe
OPO3H2
Me
CH
CH2
O
N
O
O
O
Me
HO
Me
O
Me
OH
OMe
O
MeO
Me
Me
Me

L8 ANSWER 1 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 124:250930 MARPAT Full-text
TI Hindered N-oxide esters of rapamycin
IN Nelson, Frances C.; Schiehser, Guy A.
PA American Home Products Corporation, USA
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5491231	A	19960213	US 1994-345972	19941128
	US 5508290	A	19960416	US 1995-449167	19950524
	US 5508285	A	19960416	US 1995-449168	19950524
	US 5521194	A	19960528	US 1995-450769	19950524
	US 5559122	A	19960924	US 1995-448843	19950524
	CA 2205577	AA	19960606	CA 1995-2205577	19951122
	WO 9616967	A1	19960606	WO 1995-US15318	19951122
	W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9642877	A1	19960619	AU 1996-42877	19951122
	AU 712998	B2	19991118		
	EP 794955	A1	19970917	EP 1995-941467	19951122
	EP 794955	B1	20010725		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	BR 9509825	A	19970930	BR 1995-9825	19951122
	HU 77139	A2	19980302	HU 1997-1851	19951122
	JP 10509977	T2	19980929	JP 1995-518953	19951122
	NZ 297661	A	20000128	NZ 1995-297661	19951122
	AT 203539	E	20010815	AT 1995-941467	19951122
	ES 2158959	T3	20010916	ES 1995-941467	19951122
	PT 794955	T	20011228	PT 1995-941467	19951122
	FI 9702240	A	19970527	FI 1997-2240	19970527
	HK 1002281	A1	20011102	HK 1998-101292	19980219
	GR 3036712	T3	20011231	GR 2001-401569	20010926
PRAI	US 1994-345972	19941128			
	WO 1995-US15318	19951122			

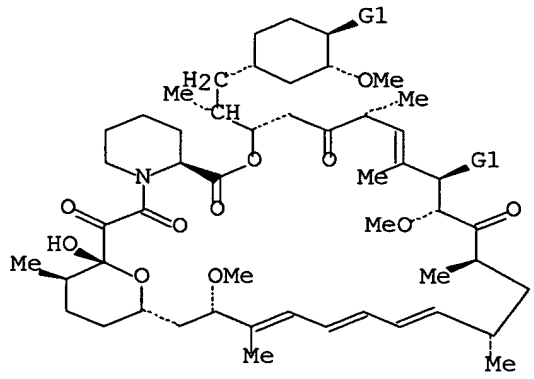
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A compound I is disclosed [R, R1 = C(O)(CH2)kC(R2)(R3)(CH2)nR4, C(O)(CH2)mC(R5)(R6)R7, H; R2, R3 = alkyl, arylalkyl, or R2 and R3 may be taken together to form cycloalkyl ring; R4 = (optionally substituted) heterocyclic N-oxide radical; R5 = alkyl, arylalkyl; R6 and R7 together form (optionally substituted) saturated N-alkyl heterocyclic N-oxide; k = 0, 1, m = 0, 1; n = 1-6; with the proviso that R and R1 are not both hydrogen], which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Preparation of

rapamycin 42-ester with 2,2-dimethyl-3-(3-pyridinyl) propionic acid N-oxide is described; the compound was tested in e.g. a standard procedure measuring lymphocyte proliferation as a measure of the immunosuppressive effect.

MSTR 1A



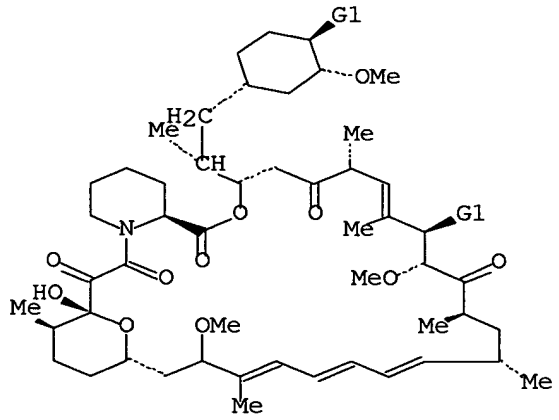
G1 = (-1) OH
G10 = PO3H2
MPL: claim 1
NTE: substitution is restricted
NTE: also incorporates broader disclosure

L8 ANSWER 2 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 124:175686 MARPAT Full-text
TI Carbamates of rapamycin
IN Kao, Wenling; Abou-Gharbia, Magid A.; Vogel, Robert L.
PA American Home Products Corporation, USA
SO U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5480989	A	19960102	US 1994-297663	19940901
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5530007	A	19960625	US 1995-402590	19950313
	US 5559120	A	19960924	US 1995-402571	19950313
	US 5508399	A	19960416	US 1995-450835	19950525
	US 5530121	A	19960625	US 1995-451104	19950525
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	US 1993-160984	19931201			
	US 1994-297663	19940901			

AB Rapamycin 42-carbamates with aminoalkanes and nitrogen heterocycles (>50 compds.) were prepared as immunosuppressants. Thus, rapamycin was esterified by ClCO2C6H4(NO2)-4 and this carbonate amidated with N,N-diethylethylenediamine to give rapamycin 42-(2-diethylaminoethyl)carbamate (I). I.HCl salt was evaluated for immunosuppressive activity in in vivo pinch skin graft and showed a survival time of 13.6 days at 4 mg/kg vs. controls which were 6-7 days.

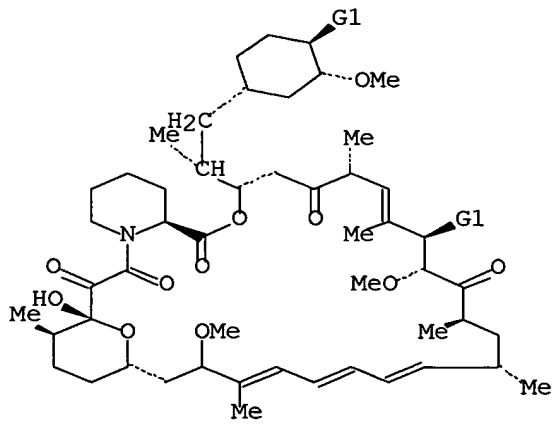
MSTR 1



G1 = (-1) OH
G13 = 145

DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

MSTR 2



G1 = (-1) OH
G13 = 145

DER: or pharmaceutically acceptable salts
MPL: disclosure

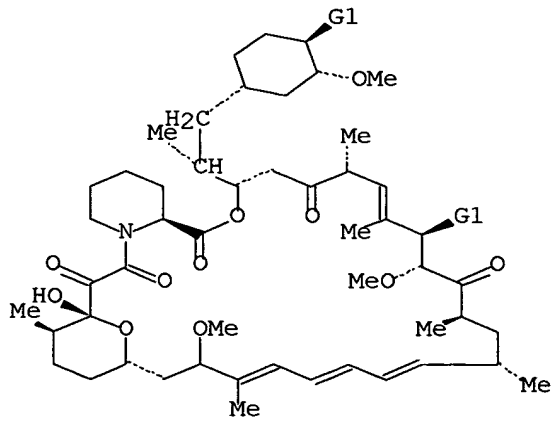
L8 ANSWER 3 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 124:145748 MARPAT Full-text
TI Carbamates of rapamycin
IN Failli, Amedeo A.; Bleyman, Oleg I.; Kao, Wenling; Abou-Gharbia, Magid A.
PA American Home Products Corporation, USA
SO U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5480988	A	19960102	US 1994-284764	19940802
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5486522	A	19960123	US 1995-448709	19950524
	US 5486524	A	19960123	US 1995-449166	19950524
	US 5486523	A	19960123	US 1995-449444	19950524
	US 5504204	A	19960402	US 1995-449453	19950524
	US 5550133	A	19960827	US 1995-448869	19950524
	US 5559227	A	19960924	US 1995-449593	19950524

PRAI US 1992-960597 19921013
US 1993-54655 19930423
US 1993-160984 19931201
US 1994-284764 19940802

AB Rapamycin 42-carbamates with alkyn- and alkenamines (10 compds.) were prepared and tested for immunosuppressant and antiinflammatory activity. Thus, rapamycin was esterified by ClCO2C6H4(NO2)-4 and this carbonate amidated with 3-(N-methyl-N-prop-2-ynylamino)propylamine to give rapamycin 42-[3-(N-methyl-N-prop-2-ynylamino)propyl] carbamate (I). I-methanesulfonate was evaluated for immunosuppressive activity in in vivo pinch skin graft and showed a survival time of 11.0 days at 4 mg/kg vs. controls which were 6-7 days. In adjuvant arthritis standard pharmacol. test I-methane sulfonate demonstrated better activity than rapamycin in treating or inhibiting rheumatoid arthritis.

MSTR 2



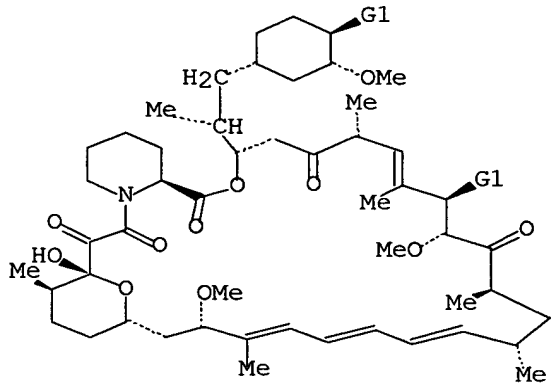
G1 = (-1) OH
G13 = 145

L8 ANSWER 4 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 123:285648 MARPAT Full-text
TI Carbamates of rapamycin
IN Skotnicki, Jerauld S.; Palmer, Yvette L.; Kao, Wenling; Abou-Gharbia, Magid A.
PA American Home Products Corporation, USA
SO U.S., 9 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

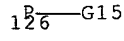
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434260	A	19950718	US 1994-259701	19940614
	US 5302584	A	19940412	US 1993-54655	19930423
	US 5516780	A	19960514	US 1995-391400	19950227
	US 5519031	A	19960521	US 1995-391398	19950227
	US 5532355	A	19960702	US 1995-395012	19950227
	US 5559119	A	19960924	US 1995-391399	19950227
	US 5559112	A	19960924	US 1995-395402	19950227
	US 5567709	A	19961022	US 1995-395013	19950227
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	US 1993-160984	19931201			
	US 1994-259701	19940614			

AB 42-O-esters of heterocyclic carbamic acids were prepared Thus, rapamycin was converted to its 42-O-(4-nitrophenoxycarbonyl) derivative which was treated with 5-phenyl-1,4,5,6-tetrahydropyrimidine hydrochloride to give the rapamycin 42-O-ester with 5-phenyl-1,4,5,6-tetrahydropyrimidine-1- carboxylic acid. The latter compound had an immunosuppressive IC50 of 0.54 nM in the test using BAB/c donor skin grafts in C2H(H-2K) mice.

MSTR 2



G1 = (-1) OH
G6 = 126



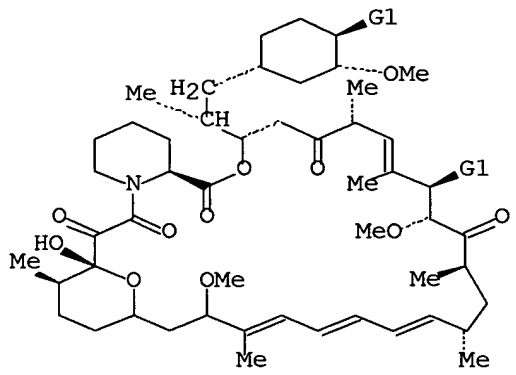
DER: or pharmaceutically acceptable salts
MPL: disclosure
NTE: alkylene in G14 may be interrupted

L8 ANSWER 5 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 123:83100 MARPAT Full-text
TI Carbamates of rapamycin
IN Kao, Wenling; Skotnicki, Jerauld S.; Abou-Gharbia, Magid A.; Palmer, Yvette L.
PA American Home Products Corporation, USA
SO U.S., 25 pp. Cont.-in-part of U.S. Ser. No. 160,984, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5411967	A	19950502	US 1994-224893	19940408
	US 5302584	A	19940412	US 1993-54655	19930423
PRAI	US 1992-960597		19921013		
	US 1993-54655		19930423		
	US 1993-160984		19931201		

AB 42- And/or 31-esters of rapamycin with carbamic acids are useful as immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agents. Thus, rapamycin was treated with 4-O2NC6H4O2CCl to give the 42-p-nitrophenyl carbonate which was treated with NH3 to give the 42-carbamate. The latter compound had an IC50 in the lymphocyte proliferation test of 1.7 nM.

MSTR 2



G1 = OH
G4 = 73

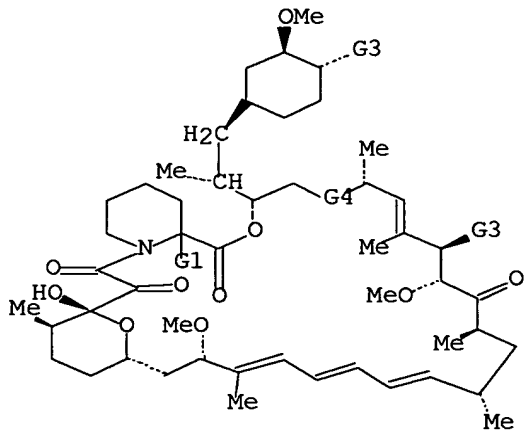
DER: or pharmaceutically acceptable salts
MPL: disclosure
NTE: substitution is restricted

L8 ANSWER 6 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 122:314360 MARPAT Full-text
TI C-22 ring stabilized rapamycin derivatives
IN Nelson, Frances C.
PA American Home Products Corp., USA
SO U.S., 22 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5387680	A	19950207	US 1993-105090	19930810
	CA 2169277	AA	19950216	CA 1994-2169277	19940810
	WO 9504738	A1	19950216	WO 1994-US9041	19940810
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9475601	A1	19950228	AU 1994-75601	19940810
	AU 676086	B2	19970227		
	EP 713490	A1	19960529	EP 1994-925809	19940810
	EP 713490	B1	19980225		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	BR 9407236	A	19960924	BR 1994-7236	19940810
	CN 1132512	A	19961002	CN 1994-193603	19940810
	HU 74675	A2	19970128	HU 1996-298	19940810
	JP 09501436	T2	19970210	JP 1995-506598	19940810
	AT 163420	E	19980315	AT 1994-925809	19940810
	ES 2115255	T3	19980616	ES 1994-925809	19940810
	PL 178625	B1	20000531	PL 1994-312991	19940810
	RU 2152946	C1	20000720	RU 1996-107113	19940810
	CZ 291205	B6	20030115	CZ 1996-358	19940810
PRAI	US 1993-105090	19930810			
	WO 1994-US9041	19940810			

OS CASREACT 122:314360
AB This invention provides C-22 substituted rapamycin derivs. and pharmaceutically acceptable salts thereof which are useful for inducing immunosuppression.

MSTR 1

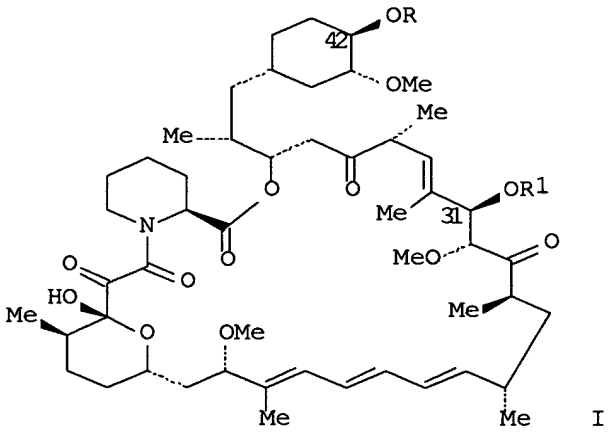


G3 = OH
G4 = C(O)
G13 = PO3H2
DER: or pharmaceutically acceptable salts
MPL: claim 6
NTE: substitution is restricted

L8 ANSWER 7 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 122:265180 MARPAT Full-text
TI Immunosuppressant gem-disubstituted esters of rapamycin
IN Ocain, Timothy D.; Schiehser, Guy A.
PA American Home Products Corp., USA
SO U.S., 14 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5385910	A	19950131	US 1993-156334	19931122
PRAI US 1993-156334	19931122			

GI

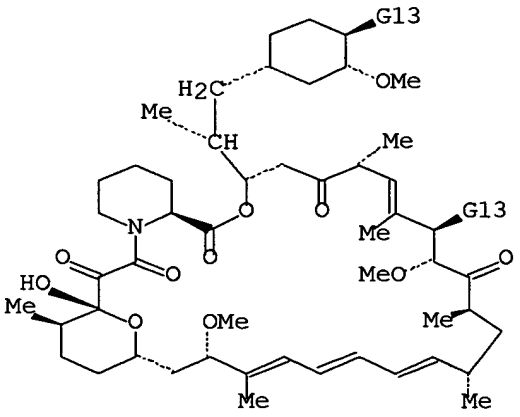


I

AB A compound of the structure I wherein R and R1 are each, independently, hydrogen, or CO(CH2)mCR2R3(CH2)nNR4R5; R2 and R3 are each, independently, alkyl of 1-6 carbon atoms, arylalkyl of 7-10 carbon atoms, or may be taken together to form a cycloalkyl ring of 3-8 carbon atoms; R4 and R5 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, arylalkyl of 7-10 carbon atoms, or may be taken together to form a saturated heterocycle having 3-6 carbon atoms selected from the group consisting of piperidine, morpholine, thiomorpholine, piperazine, pyrazolidine, imidazolidine, and pyrrolidine, wherein the heterocyclic ring may be optionally mono-, di-, or tri-substituted with a group selected from alkyl of 1-6 carbon atoms and perfluoroalkyl of 1-6 carbon atoms; wherein the aryl moiety of the arylalkyl group of R2, R3, R4, and R5 is, e.g., Ph, naphthyl, pyridinyl; m=0-1; and n=0-6; with the proviso that R and R1 are not both hydrogen, or a pharmaceutically acceptable salt thereof which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte

proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2-amino-2-methylpropionic acid maleate salt, LAF IC50 : 5.3 and 8.4 nM; skin graft survival time: 12.0 ± 0.0 and 11.0 ± 0.9 days; percent change in adjuvant arthritis vs. control: -73%; heart allograft survival time: 19.11 days. Pharmaceutical formulations were given.

MSTR 1

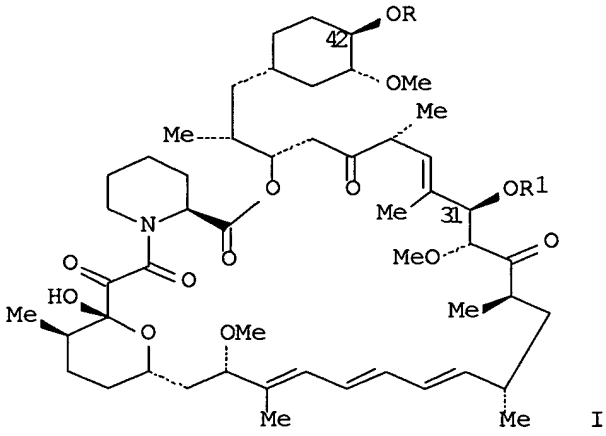


G6 = PO3H2
G13 = (-1) OH
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: includes broader disclosure

L8 ANSWER 8 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 122:265179 MARPAT Full-text
TI Heterocyclic esters of rapamycin
IN Nelson, Frances C.; Schiehser, Guy A.
PA American Home Products Corp., USA
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5385909	A	19950131	US 1993-156208	19931122
	CA 2176961	AA	19950601	CA 1994-2176961	19941116
	WO 9514697	A1	19950601	WO 1994-US13411	19941116
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9510571	A1	19950613	AU 1995-10571	19941116
	EP 730597	A1	19960911	EP 1995-901258	19941116
	EP 730597	B1	20010307		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09505596	T2	19970603	JP 1994-515166	19941116
	AT 199555	E	20010315	AT 1995-901258	19941116
	ES 2154720	T3	20010416	ES 1995-901258	19941116
	PT 730597	T	20010629	PT 1995-901258	19941116
	HK 1011354	A1	20010622	HK 1998-112278	19981124
	GR 3035835	T3	20010831	GR 2001-400683	20010507
PRAI	US 1993-156208	19931122			
	WO 1994-US13411	19941116			

GI

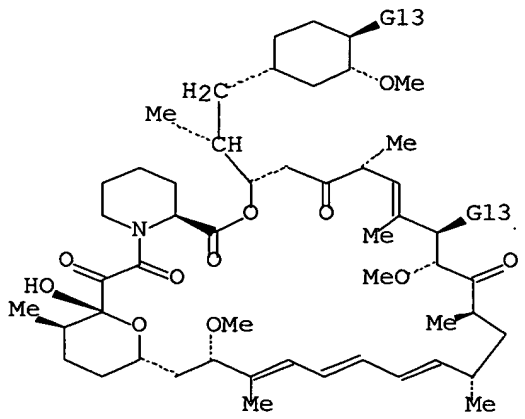


I

AB A compound of the structure I wherein R and R1 are each, independently, CO(CH2)nR2 or hydrogen, R2 is a heterocyclic radical which may be optionally substituted; n=0-6; with the proviso that R and R1 are both not hydrogen, or a pharmaceutically acceptable salt thereof which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro

standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2-methylnicotinic acid: LAF IC50 = 1.00 nM; skin graft survival: 11.2 ± 0.8 days; percent change in adjuvant arthritis vs. control: -88%; heart allograft survival: 29.9 days, i.p. Pharmaceutical formulations were given.

MSTR 1



G6 = PO3H2
G13 = (-1) OH
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: includes broader disclosure

L8 ANSWER 9 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 122:265178 MARPAT Full-text
TI Immunosuppressant hindered esters of rapamycin
IN Nelson, Frances C.; Schiehser, Guy A.
PA American Home Products Corp., USA
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5385908	A	19950131	US 1993-156206	19931122
	CA 2176955	AA	19950601	CA 1994-2176955	19941118
	WO 9514696	A1	19950601	WO 1994-US13310	19941118
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9512575	A1	19950613	AU 1995-12575	19941118
	EP 730598	A1	19960911	EP 1995-903559	19941118
	EP 730598	B1	19990609		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09505592	T2	19970603	JP 1994-515148	19941118
	AT 181076	E	19990615	AT 1995-903559	19941118
	ES 2133715	T3	19990916	ES 1995-903559	19941118
	SG 80525	A1	20010522	SG 1996-2897	19941118
	HK 1013063	A1	20000428	HK 1998-112277	19981124
PRAI	US 1993-156206	19931122			
	WO 1994-US13310	19941118			

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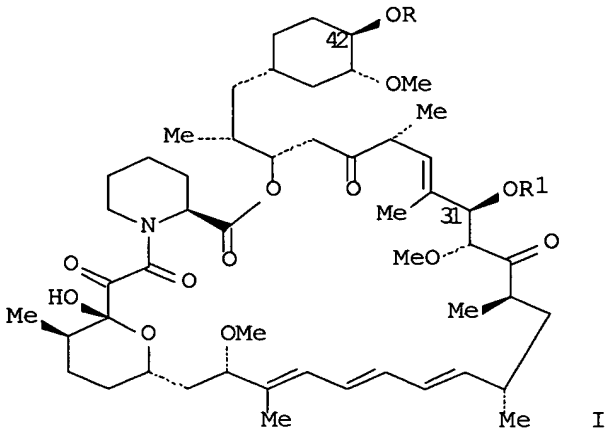
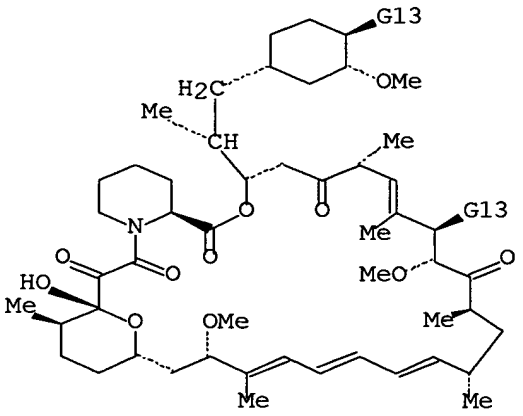


I

AB A compound of the structure I wherein R and R1 are each, independently, CO(CH2)kCR2R3(CH2)nR4, CO(CH2)mCR3R5R6, or hydrogen; R2 and R3 are each, independently, alkyl, arylalkyl, or R2 and R3 may be taken together to form a cycloalkyl ring; R4 is a heterocyclic radical which may be optionally substituted; R5 is alkyl or arylalkyl; R6 and R7 are taken together to form a saturated heterocyclic ring which may be optionally substituted; k=0-1, m=0-1; n=1-6; with the proviso that R and R1 are not both hydrogen, or a pharmaceutically acceptable salt thereof, which is

useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in three in vivo standard pharmacol. test procedures. Thus, e.g., for rapamycin 42-ester with 2,2-dimethyl-3-(3-pyridinyl) propionic acid, LAF IC50: 0.83 nM; skin graft survival: 13.6 ± 0.6 days; percent change in adjuvant arthritis vs. control: -62%; heart allograft: 29 days, i.p.; 11.5 days, p.o. Pharmaceutical formulations were given. Safety note: authors identify 3-picolyl chloride as a lachrymator.

MSTR 1



G6 = PO3H2
G13 = (-1) OH
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: includes broader disclosure

L8 ANSWER 10 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 122:213858 MARPAT Full-text
TI Preparation of rapamycin conjugates for generation of antibodies
IN Molnar-Kimber, Katherine Lu; Ocain, Timothy Donald; Caufield, Craig Eugene; Caggiano, Thomas Joseph; Failli, Amedeo Arturo
PA American Home Products Corp., USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9425072	A1	19941110	WO 1994-US4463	19940422
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9467119	A1	19941121	AU 1994-67119	19940422
	EP 1181938	A2	20020227	EP 2001-120777	19940422
	EP 1181938	A3	20020320		
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	US 6328970	B1	20011211	US 2000-576952	20000524
	US 2001010920	A1	20010802	US 2001-773562	20010202
	US 6541612	B2	20030401		
	US 2002151088	A1	20021017	US 2002-124386	20020418
	JP 2004149542	A2	20040527	JP 2003-412072	20031210
	JP 2004168782	A2	20040617	JP 2003-412071	20031210
PRAI	US 1993-53030	19930423			
	US 1994-224207	19940414			
	US 1994-224205	19940414			
	EP 1994-915854	19940422			
	JP 1994-524408	19940422			
	WO 1994-US4463	19940422			
	US 1995-424983	19950419			
	US 2000-576951	20000524			
	US 2000-576952	20000524			

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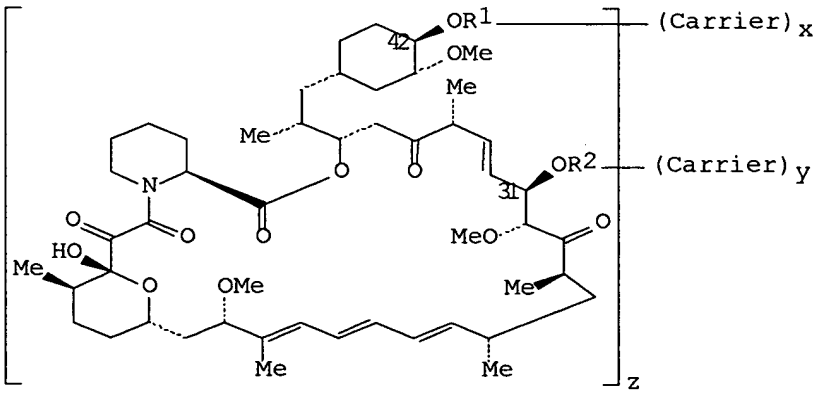
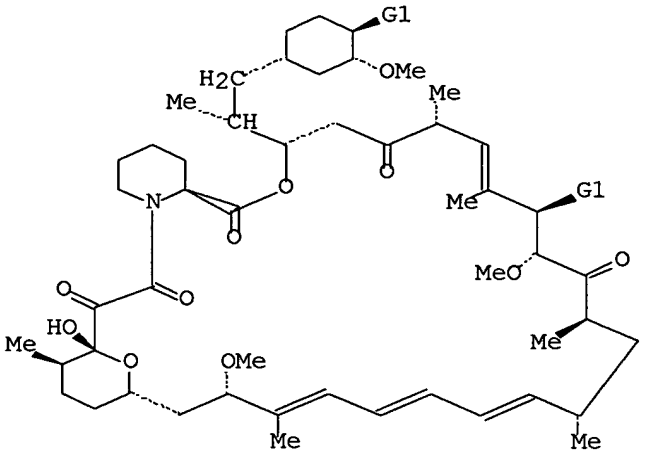


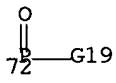
I

AB Title compds. I [(R1, R2 = H, (R3LR4) wherein L = linking group, R3 = CO, SO, SO2, PO2, POMe,CS, CH2CO; R4 = CO, NH, S, CH2, O; a = 1-5; z = 1-120), carrier = immunogenic material, detector material, solid matrix, salt; x, y = 0,1 with provisos], are prepared Succinic anhydride and dimethylaminopyridine were added to II to give II 42-ester with succinic acid which was treated with N-hydroxysuccinimide to give II 42-ester with N-hydroxysuccinimide hemisuccinate which was conjugated with proteins and horseradish peroxidase. Screening for monoclonal antibodies specific for II or its derivs. as well as immunoassay are given.

MSTR 1



G1 = (-1) OH
G3 = 72

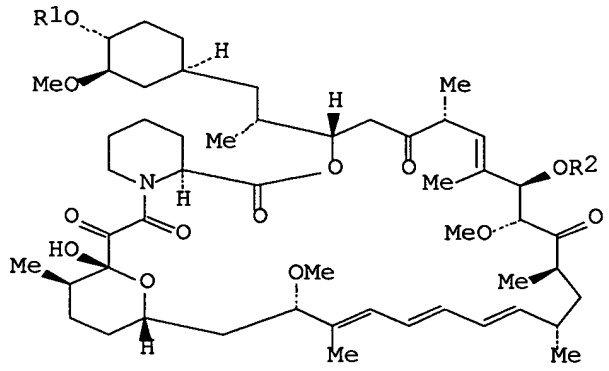


DER: or salts
MPL: claim 1

L8 ANSWER 11 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 121:179406 MARPAT Full-text
TI Preparation of O-(imidazolylalkyl)rapamycins and analogs as immunosuppressants and antimicrobials
IN Goulet, Mark; Parsons, William H.; Wyvratt, Matthew J.
PA Merck and Co., Inc., USA
SO U.S., 35 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5310903	A	19940510	US 1993-26925	19930305
PRAI	US 1993-26925	19930305			

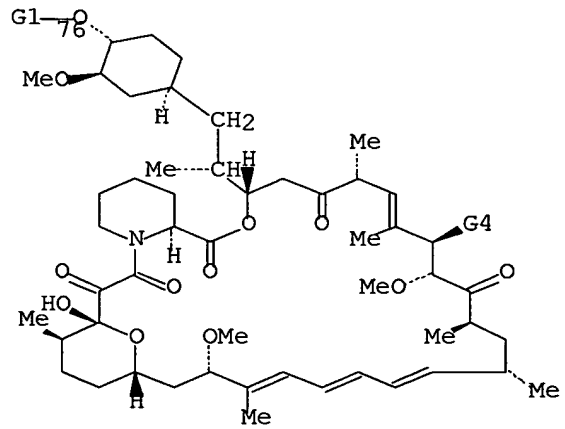
GI



I

AB Title compds. [I; R1 = (un)substituted 2-imidazolylmethyl, -benzyl, etc.; R2 = H, groups cited for R1, etc.] were prepared as immunosuppressants and antimicrobials (no data). Thus, rapamycin was converted in 3 steps to 42-(2-oxoethoxy)rapamycin which was cyclocondensed with phenylglyoxal and NH3 to give 42-[(4-phenyl-2-imidazolyl)methoxy]rapamycin.

MSTR 1



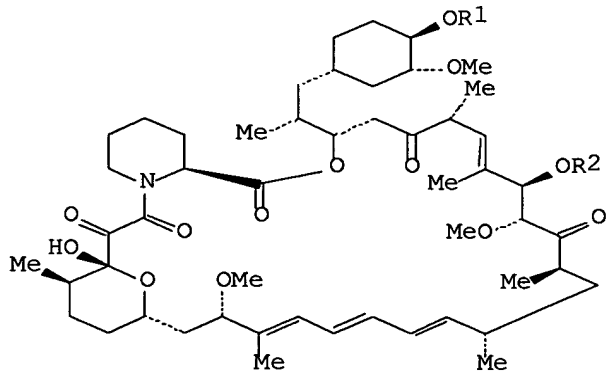
G4 = OH
G7 = PO3H2
DER: or pharmaceutically acceptable salts

MPL: claim 1
NTE: Ak in G16 and alkylene in G17 may be optionally interrupted

L8 ANSWER 12 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 121:108376 MARPAT Full-text
TI Preparation of rapamycin carbamates
IN Kao, Wenling; Abou-Gharbia, Magid Abdel; Vogel, Robert Lewis
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 593227	A1	19940420	EP 1993-308040	19931008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5302584	A	19940412	US 1993-54655	19930423
	EP 1266900	A1	20021218	EP 2002-14573	19931008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
PRAI	US 1992-960597	19921013			
	US 1993-54655	19930423			
	GB 1993-17596	19930824			
	EP 1993-308040	19931008			

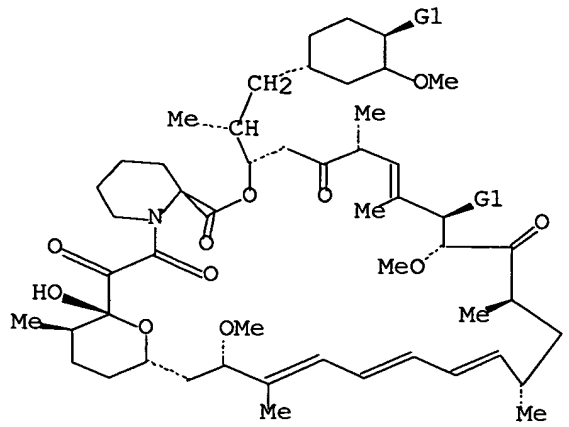
GI



I

AB Title compds. I (R1, R2 = H, -CONH-[(CR3R4)m(-A-(CR5R6)n)p]q-B, R9R10NCO, (substituted) heterocyclyl; R3, R4, R5, R6, R9 and R10 = H, C1-6 alkyl, C2-7 alkenyl, C2-7 alkynyl, hydroxy-C1-6 alkyl, etc.; B = C2-7 alkenyl, C2-7 alkynyl, Ho-C1-6 alkyl, C2-12 alkylthioalkyl, etc.; A = CH2, O, S, SO, R7N, R7P, NHCO, NHSO, R7PO eherein R7 = H, C1-6 alkyl, C7-10 aralkyl, alkyl(dialkyl)aminoalkyl, etc.; m, n = 0-6; p, q = 0,1) or a salt thereof, useful as immunosuppressants (data) antiinflammatories, antiproliferating and antitumor agents (no data), are prepared I [R1 = p-(O2N)C6H4CO2, R2 = H] in CH2Cl2 was treated at -10° under N with 2-(2- aminoethyl)pyridine to give after workup I [R1 = 2-(pyridin-2- yl)ethylcarbamoyl, R2 = H] which was converted to the HCl salt (II). In an in vivo test for evaluating immunosuppressive activity, the survival time of pinch skin graft of II at 4 mg/kg was 11.40 days vs. controls which was 6-7 days.

MSTR 1



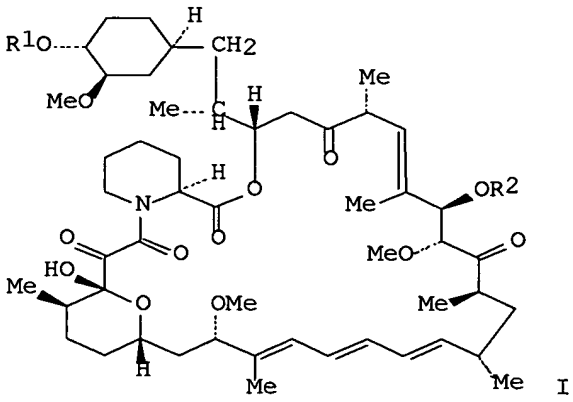
G1 = (-1) OH
G4 = 71

DER: and pharmaceutically acceptable salts
MPL: claim 1

L8 ANSWER 13 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 121:73883 MARPAT Full-text
TI O-heteroaryl, O-alkylheteroaryl, O-alkenylheteroaryl and O-alkynylheteroarylrapamycin derivatives for treatment of autoimmune, inflammatory, and other diseases
IN Parsons, William H.; Sinclair, Peter J.; Wong, Frederick; Wyvratt, Matthew J.
PA Merck and Co., Inc., USA
SO U.S., 34 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5310901	A	19940510	US 1993-26926	19930305
PRAI US 1993-26926	19930305			

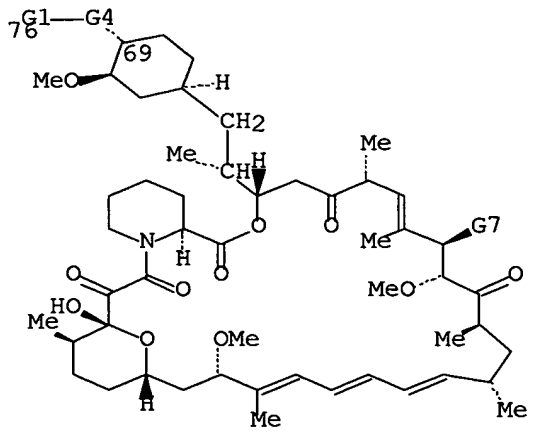
GI



I

AB O-heteroaryl, O-alkylheteroaryl, O-alkenylheteroaryl and O-alkynylheteroarylrapamycin derivs. I (R1 = heteroaryl, substituted heteroaryl, heteroaryl-C1-10 alkyl, etc.; R2 = R1, H, Ph, substituted Ph, 1- or 2-naphthyl, etc.) have been prepared from suitable precursors by alkylation and/or arylatin at C-42 and/or C-31. These compds. are useful in a mammalian host for the treatment of autoimmune diseases and diseases of inflammation, infectious diseases, the prevention of rejection of foreign organ transplants, and the treatment of solid tumors. Preparation of selected I is included. 42-(1-Hydroxyethylindol-5-yl)oxyrapamycin inhibited proliferation of T-cells.

MSTR 1

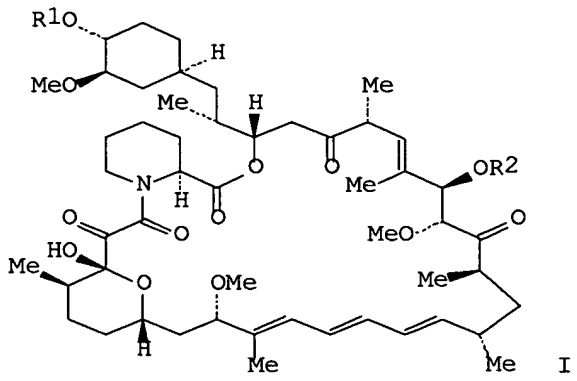


G7 = OH
G10 = PO3H2
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: alkylene and alkenylene in G5 and ak in G6 may be optionally interrupted

L8 ANSWER 14 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 120:217095 MARPAT Full-text
TI Preparation of O-aryl, O-alkyl, O-alkenyl and O-alkenylrapamycin derivatives
IN Goulet, Mark; Parsons, William H.; Sinclair, Peter J.; Wong, Frederick; Wyvratt, Matthew J.
PA Merck and Co., Inc., USA
SO U.S., 21 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5258389	A	19931102	US 1992-973807	19921109

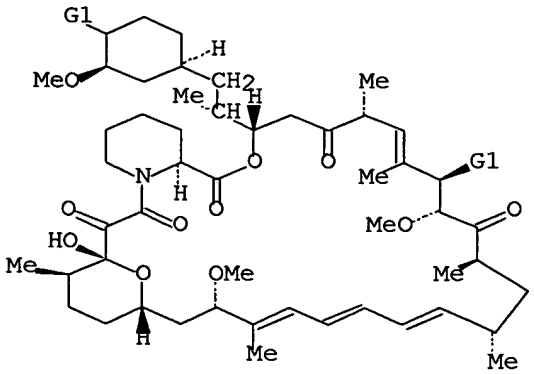
PRAI US 1992-973807 19921109
GI



I

AB Title compds. I (R1, R2 = H, optionally substituted Ph, naphthyl, biphenyl, C1-10 alkyl, C3-10 alkenyl, C3-10 alkynyl) useful for treatment of autoimmune diseases, inflammation, infectious prevention of rejection of transplants (no data) and solid tumor, are prepared To Ph3Bi in CH2Cl2 was added AcO2H followed by THF, rapamycin and Cu(OAc)2 to give I (R1 = Ph, R2 = H) (II). II and other derivs. of I inhibited T-cell proliferation.

MSTR 1



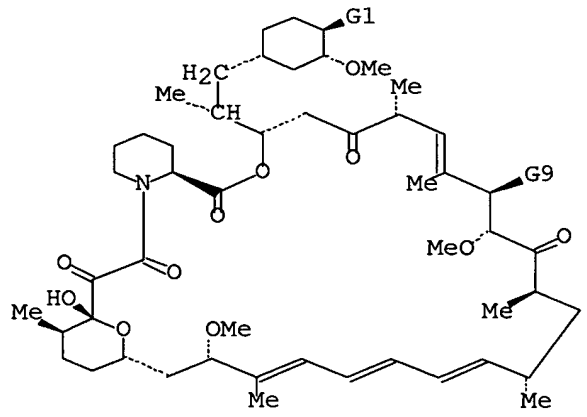
G1 = (-1) OH
G16 = PO3H2
DER: or pharmaceutically acceptable salts
MPL: claim 1

L8 ANSWER 15 OF 15 MARPAT COPYRIGHT 2005 ACS on STN
AN 118:80729 MARPAT Full-text
TI (carbamoyl)rapamycin derivatives, a method for their preparation and their use as immunosuppressants
IN Kao, Wenling; Vogel, Robert Lewis; Musser, John Henry
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 509795	A2	19921021	EP 1992-303401	19920415
	EP 509795	A3	19940323		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	US 5118678	A	19920602	US 1991-686728	19910417
	US 5194447	A	19930316	US 1992-837048	19920218
	CA 2065791	AA	19930819	CA 1992-2065791	19920410
	US 5262424	A	19931116	US 1992-977380	19921117
PRAI	US 1991-686728	19910417			
	US 1992-837048	19920218			

OS CASREACT 118:80729
AB Some rapamycin carbamate derivs. are claimed. Pharmaceuticals containing said compds. are claimed. A mixture of rapamycin, pyridine, and 4-fluorophenyl isocyanate was stirred at 0° for 5 h to give rapamycin 42-[(4-fluorophenyl)carbamate] (I). The immunosuppressant activity of I was demonstrated in a thymocyte proliferation test, mixed lymphocyte reaction and in the survival of a pinch skin graft on mice.

MSTR 1A



G7 = PO3H2
G9 = OH
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

```
=> d l1; d his; log y
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.



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L3           14 S L1 FUL

     FILE 'CAPLUS' ENTERED AT 16:56:18 ON 15 FEB 2005
L4            5 S L3

     FILE 'MARPAT' ENTERED AT 16:57:00 ON 15 FEB 2005
L5            0 S L3
L6           18 S L3 FUL
L7           18 S L1 FUL
L8           15 S L7 NOT L4


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FULL ESTIMATED COST                               241.71     428.40

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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